REMARKS

Claims 2-7, 9 and 11 are pending; claims 4-7 and 9 have been withdrawn from consideration; claims 2, 3 and 11 have been rejected.

The claims are being amended, in part, to correct the dependency of the claims. Because claims 2-7 improperly depend on a claim of a higher number (claim 11), these claims are being canceled and replaced by new claims 12-17. New claims 12-17 thus correspond to canceled claims 2-7, respectively.

Support for the amendment of claim 11 to recite a vaccine comprising a tumor cell may be found in paragraph [0016]. Support for the amendment of claim 11 to include a third component (a virus for immunological treatment) may be found in canceled claim 4.

Support for new claim 18 may be found in the second sentence of paragraph [0014], and in paragraph [0012].

Support for new claim 19 may be found in paragraph [0018].

Support for new claim 20 may be found in the last two sentences of paragraph [0014].

No new matter has been added. Entry of the amendment is respectfully requested.

I. Information Disclosure Statement

The Examiner states that the listing of non-patent literature on the IDS document list submitted February 26, 2010 is incomplete because the title of documents with citation numbers 1-6 was not provided. The Examiner indicates that the entirety of each document has been considered (the Examiner states that the documents are considered to "the extent of the information documented on the IDS" which includes sufficient information to identify each document from among the non-patent literature documents filed with the IDS).

To complete the formalities with regard to the document list, a revised document list is being filed herewith, containing the title of each listed document. Applicants respectfully request that the Examiner return an initialed and signed copy of the document list, confirming consideration of the six non-patent literature documents set forth thereon.

II. Rejection Under 35 U.S.C. §103

A. At paragraph 2 of the office action, claims 2, 3, and 11 remain rejected as being unpatentable under 35 U.S.C. §103(a) over Nanni et al. (2001) in view of Hamada et al. (2003). The Examiner states that the rejection has been maintained for the reasons first set forth in the office action dated September 4, 2008. Such reasons are repeated at pages 5-7 of the office action.

In response, Applicants respectfully assert that the Examiner has not established a *prima facie* showing of obviousness under 35 U.S.C. 103 and traverse the Examiner's position for the following reasons.

First, Applicants note that included herewith is an amendment to the claims such that claim 11 now recites a kit comprising three components: (i) a vaccine that comprises a tumor cell, (ii) a carrier cell infected with an oncolytic virus, and (iii) a virus for immunological treatment. The combination of Nanni and Hamada does not teach such a kit. Nanni teaches the administration of tumor cells (Neu/H-2^q cells) and IL-12 alone. Hamada teaches administration of oncolytic virus (AdE3-*IA1.3b*) alone. The combination of the two documents does not teach, *inter alia*, the use of a virus for immunological treatment, nor does the combination of documents suggest the use of this third component of the claimed kit.

Second, the skilled artisan would not have been motivated to combine the teachings of Nanni and Hamada.

The Examiner contends that Nanni teaches a tumor cell, and that Hamada teaches an A549 cell infected with an oncolytic virus, and that it would have been *prima facie* obvious to combine the two disclosures. Applicants respectfully assert that the skilled artisan would not have had a motivation to combine the tumor cells of Nanni with the virus-infected cells of Hamada to produce a kit comprising these components.

In particular, the Examiner states in the office action that the skilled artisan would have been motivated to combine the teachings of Nanni and Hamada because "there are two different molecular mechanisms underlying the treatment of breast and ovarian cancers", with Nanni

allegedly teaching one mechanism and Hamada the other. The Examiner states that Hamada teaches a replication-selective oncolytic virus that specifically targets ovarian cancer, and that this virus is the noted "molecular mechanism" of Hamada.

While Hamada may teach a replication-selective oncolytic virus, Applicants note that the claims are directed to a kit comprising a cell that is *infected* with an oncolytic virus. Each of the methods taught in Hamada is directed to the administration of the virus directly into tumors (see, e.g., page 2507, right column, lines 2, 8-10 and 20-21). Hamada does not provide any suggestion of using a cell comprising the oncolytic virus. While Hamada teaches the infection of cells with virus, such as A549 cells (page 2510, right column, second paragraph), such cells are solely used to replicate the virus *in vitro* and not administered to a subject.

While it might be argued that the teachings of Nanni and Hamada could be combined as a kit comprising: (1) a tumor cell and (2) an oncolytic virus, such a combination is not being claimed. Instead, the present application is directed to a kit comprising: (1) a tumor cell and (2) an A549 cell infected with an oncolytic virus. And as discussed above, the kit further includes a virus for immunological treatment.

There would have been no reason for the skilled artisan to administer a virus-infected cell to a subject in Hamada. Hamada teaches the successful administration of the virus itself to a tumor. Indeed, as the virus of Hamada is being injected directly into the tumor, the skilled artisan would expect the use of cells infected with the virus to introduce an unnecessary obstacle in the method of treatment being disclosed. The virus would need to replicate in the cell and then lyse the cell in order to be able to infect cells of the tumor. As Hamada reveals very good results through the administration of the virus directly into the tumor, the skilled artisan would not have paired a cell infected with the virus with the tumor cells recited in the kit claims of the pending application.

Third, the skilled artisan would not have had a reasonable expectation of success in combining the disclosures of Nanni and Hamada.

While the Examiner suggests that there would have been a reasonable expectation of success in combining the disclosures of Nanni and Hamada, Applicants note again that the Examiner states Hamada teaches the successful use of an oncolytic virus, and bases his reasoning on this teaching. However, Hamada does not teach the administration of a cell infected with an oncolytic virus into a tumor.

Applicants respectfully assert that this distinction is substantial. By administering the oncovirus directly, the virus is able to immediately bind, enter and lyse target tumor cells. While the host immune system will also be immediately activated upon injection of the virus, because "naked" virus is administered it can swiftly bind the tumor cells before the host immune system has the opportunity to eliminate the virus. If cells infected with the virus are administered to the subject, such cells may be eliminated prior to the release of viral particles in sufficient quantities to have a significant effect on the tumor cells. There is nothing in Hamada (or Nanni) to suggest that the skilled artisan would have had a reasonable expectation of success in combining the tumor cells of Nanni with the cells infected with a virus of Hamada. Indeed, prior to the disclosure of the combined potency of the elements of the kit being claimed in the pending application, the skilled artisan would have had no expectation of success in preparing a kit comprising these elements.

It should also be noted that Nanni teaches means of preventing development of tumors in an animal (see, e.g., page 1196, column 1, first sentence of first full paragraph; page 1200, first sentence of the Discussion). In contrast, as shown in the examples of the pending application, the kit can be used to treat existing tumors in an animal. The skilled artisan might reasonably expect that inhibition of tumor development would be much easier to achieve than the destruction of a fully-formed tumor. In the former, one would simply need to destroy individual cells as they develop. Such cells would not have the features of a fully-formed tumor, such as a capsule or extensive vasculature. In the latter, one would need to adapt the therapy to address these characteristics of a fully-formed tumor. The Examiner has not pointed to any teaching in Nanni (or Hamada) to suggest that administration of tumor cells could also be used to treat tumors, in addition to simply preventing their formation.

For these reasons Applicants respectfully maintain that a *prima facie* showing of obviousness has not been established. Applicants therefore request consideration and withdrawal of the rejection.

B. At paragraph 3 of the office action, claims 2, 3, and 11 remain rejected as being unpatentable under 35 U.S.C. §103(a) over Nanni et al. (2001) in view of Tsukuda et al. (2002) and Barker (1999). The Examiner states that the rejection has been maintained for the reasons first set forth in the office action dated September 4, 2008.

In response, Applicants respectfully assert that the Examiner has not established a *prima facie* showing of obviousness under 35 U.S.C. 103 and traverse the Examiner's position for the following reasons.

First, Applicants again note that included herewith is an amendment to the claims such that claim 11 now recites a kit comprising three components: (i) a vaccine that comprises a tumor cell, (ii) a carrier cell infected with an oncolytic virus, and (iii) a virus for immunological treatment. The combination of Nanni, Hamada and Barker does not teach such a kit. Nanni teaches the administration of tumor cells (Neu/H-2^q cells) and IL-12 alone. Hamada and Barker each teach administration of an oncolytic virus (AdE3-*IA1.3b* and Ad*E2F-1*^{RC}, respectively) alone. The combination of the three documents does not teach the use of a virus for immunological treatment, nor does the combination of documents suggest the use of this third component of the claimed kit.

Second, the skilled artisan would not have been motivated to combine the teachings of Nanni, Hamada and Barker. Applicants incorporate the arguments on this point above with regard to the rejection over Nanni and Barker alone. Applicants further note that, as with Hamada, Tsukuda teaches the administration of virus alone into tumors. Tsukuda does not teach administration of cells infected with virus into the tumors. Each of the three protocols discussed in the paragraphs under "Treatment of Established Tumors with AdE2F-*1*^{RC}" in the columns on page 3440 of Tsukuda makes clear that virus alone is administered to a subject. As Tsukuda reveals very good results through the administration of the virus directly into the tumor, the

skilled artisan would not have paired a cell infected with the virus with the tumor cells recited in the kit claims of the application.

Third, the skilled artisan would not have had a reasonable expectation of success in combining the teachings of Nanni, Hamada and Barker. Applicants incorporate the arguments on this point above with regard to the rejection over Nanni and Barker alone, and further note that nothing in the combination of publications that includes Tsukuda teaches or suggests that the skilled artisan would have had a reasonable expectation of success in combining the tumor cells of Nanni with the cells infected with a virus of Hamada or Tsukuda.

For these reasons Applicants respectfully maintain that a *prima facie* showing of obviousness has not been established. Applicants therefore request consideration and withdrawal of the rejection.

III. Conclusion

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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